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A Blood-Chemical Test for Adrenal Cortex Extracts.

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The clinical picture of adrenal insufficiency in animals has been described by many authors. Certain of the blood changes have also been described, but for the most part these have been isolated or terminal findings. Our experiments have extended the chemical studies to day by day observations. We find that a fall in CO_2 capacity, a non-protein nitrogen rise, a chloride fall and a fall in blood sugar occur in experimental adrenal insufficiency. The blood-chemical picture has been correlated with observed symptoms of loss of appetite, asthenia, dehydration, and decreased peripheral circulation.

Injection of our adrenin-free extract of the adrenal cortex,[1] brings about a reversal of the shift in adrenal insufficiency. The CO_2 capacity and blood chlorides rise to normal, the non-protein nitrogen fails to rise, and the blood sugar increases. There is in adrenalectomized cats an immediate clinical improvement and their appetite for solid food returns. A few animals injected while in a comatose state, have soon after gotten up and walked around.

Even normal animals react to doses of this cortex extract and we use them to test its potency. The injection of 0.5 cc./kg. body weight of an extract in which 1 cc.=0.5 gm. of fresh whole beef adrenal, will produce a rise in carbon-dioxide capacity and in blood sugar. A fall occurs in the non-protein nitrogen, if it is high, and a rise, if it is normal. The same shift is found in the blood chlorides. Similar results have been obtained using cats, dogs and rabbits.

The maximal chemical changes are not immediate. The blood sugar reaches its high point in 1 to 5 hours; the chlorides are changed within an hour or so; the rise in carbon-dioxide capacity, which is the most significant change, occurs in about 5 hours, but takes 24 to 48 hours to reach its peak. Injections of preparations not adrenin-free produce an initial drop in the carbon-dioxide combining capacity.

The use of normal animals for tests has obviated the necessity

[1] Zwemer, R. L., Agate, F. J., and Schroeder, H. A., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 721.

for many adrenalectomies and also conserves material, since we and others[2, 3] have found that it requires huge quantities of extract to keep adrenalectomized cats alive.

As yet a lack of uniformity in test animals must be encountered. An animal with an initial low carbon-dioxide capacity will show a greater reaction to the extracts than one injected when the carbon-dioxide capacity is high.

Forty-two adrenalectomized and 51 normal cats form the basis for this paper. Tests were repeatedly made on certain of these animals. Over 400 blood chemical determinations were made on the above animals. In studying the clinical symptoms of adrenal insufficiency over 200 animals were used.

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Continuous Pancreatic Secretion.

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The following study was undertaken in order to determine the characteristics of the flow of pancreatic juice in the fasting dog and the influence of certain stimuli upon the rate of pancreatic secretion. Cl. Bernard[1] and Pavlov[2] believed that pancreatic juice was secreted intermittently in response to specific stimuli. Continuous secretion was regarded by them as an abnormal response of the pancreas to irritation and inflammation. Farrell and Ivy[3] found that pancreatic transplants secreted continuously in dogs. Recently Baxter[4] reported that spontaneous pancreatic secretion occurred in rabbits under prolonged urethane anesthesia, after decerebration or decapitation, and after extirpation of the entire gastro-intestinal tract.

Permanent pancreatic fistulas were established in 4 dogs under ether anesthesia and with strict asepsis according to the technic de-

[2] Hartman, F. A., *Endocrinol.*, 1930, **14**, 229.

[3] Swingle, W. W., and Pfiffner, J. J., *Science*, 1930, **71**, 321.

[1] Bernard, C., *Mémoire sur le pancréas.* 1856.

[2] Pavlov, I. P., The work of the digestive glands. London, C. Griffin and Co., 1910.

[3] Farrell, J. I., and Ivy, A. C., *Am. J. Physiol.*, 1926, **78**, 325.

[4] Baxter, S. G., *Am. J. Physiol.*, 1931, **96**, 343.